



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,017	12/08/2005	Rodolfo Cadilla	PU4831USW	2811
23347	7590	10/14/2008		
GLAXOSMITHKLINE CORPORATE INTELLECTUAL PROPERTY, MAI B482 FIVE MOORE DR., PO BOX 13398 RESEARCH TRIANGLE PARK, NC 27709-3398			EXAMINER POWERS, FIONA	
			ART UNIT 1626	PAPER NUMBER
			NOTIFICATION DATE 10/14/2008	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USCIPRTP@GSK.COM
LAURA.M.MCCULLEN@GSK.COM
JULIE.D.MCFALLS@GSK.COM

Office Action Summary	Application No. 10/560,017	Applicant(s) CADILLA ET AL.	
	Examiner Fiona T. Powers	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8,10,16 and 17 is/are pending in the application.
4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 8,10,16 and 17 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>12/8/05</u> . | 6) <input type="checkbox"/> Other: ____. |

Art Unit: 1626

Claims 8, 10, 16 and 17 are pending.

Receipt is acknowledged of the preliminary amendment and information disclosure statement filed December 8, 2005, which have been entered in the file.

Claim 8 is objected to because of the following informalities: in claim 8, in the definition of R^9 a space is needed between "and" and " R^9 ". Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8 , 10, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat.

Art Unit: 1626

App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 8 recites the broad recitation "a compound of Formula (I)", and the claim also recites "and the compound is selected from: N-(cyclopropylmethyl)-N-(4-nitro-1-naphthyl)-N-propylamine etc." which is the narrower statement of the range/limitation.

In claim 8, "n" is not defined.

Claim 17 is indefinite because it is drawn to a method for the treatment or prophylaxis of various diseases and disorders including "libido enhancement". However, libido enhancement is not a disease or disorder; rather it may be a desired result of treatment of a disease or disorder.

Art Unit: 1626

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph are as follows:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of skill in the art.

See In re Wands, 8 USPQ2d 1400.

Art Unit: 1626

The nature of the invention is the treatment or prophylaxis of conditions or disorders that respond to selective androgen receptor modulation and treatment or prophylaxis of osteoporosis, muscle wasting, frailty, cardiovascular disease, breast cancer, uterine cancer, prostatic hyperplasia, prostate cancer, dyslipidemia, menopausal vasomotor conditions, urinary incontinence, arteriosclerosis, libido enhancement, depression, uterine fibroid disease, aortic smooth muscle cell proliferation, endometriosis, or ADAM comprising the administration of a compound according to claim 8.

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases and by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 166 USPQ 18 indicates

Art Unit: 1626

that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicants are claiming the treatment or prevention of any condition or disorder that responds to selective androgen receptor modulation and treatment or prevention of osteoporosis, muscle wasting, frailty, all cardiovascular diseases, breast cancer, uterine cancer, prostatic hyperplasia, prostate cancer, dyslipidemia, menopausal vasomotor conditions, urinary incontinence, arteriosclerosis, libido enhancement, depression, uterine fibroid disease, aortic smooth muscle cell proliferation, endometriosis, or ADAM comprising the administration of a compound according to claim 8.

According to the specification at page 7, lines 11 to 35:

Art Unit: 1626

An aspect of the present invention is the use of the compounds of the present invention for the treatment or prophylaxis of a variety of disorders including, but not limited to, osteoporosis and/or the prevention of reduced bone mass, density, or growth, osteoarthritis, acceleration of bone fracture repair and healing, acceleration of healing in joint replacement, periodontal disease, acceleration of tooth repair or growth, Paget's disease, osteochondrodysplasias, muscle wasting, the maintenance and enhancement of muscle strength and function, frailty or age-related functional decline ("ARFD"), dry eye, sarcopenia, chronic fatigue syndrome, chronic myalgia, acute fatigue syndrome, acceleration of wound healing, maintenance of sensory function, chronic liver disease, AIDS, weightlessness, burn and trauma recovery, thrombocytopenia, short bowel syndrome, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease and ulcerative colitis, obesity, eating disorders including anorexia associated with cachexia or aging, hypercortisolism and Cushing's syndrome, cardiovascular disease or cardiac dysfunction, congestive heart failure, high blood pressure, malignant tumor cells containing the androgen receptor including breast, brain, skin, ovary, bladder, lymphatic, liver, kidney, uterine, pancreas, endometrium, lung, colon, and prostate, prostatic hyperplasia, hirsutism, acne, seborrhea, androgenic alopecia, anemia, hyperpliosity, adenomas and neoplasms of the prostate, hyperinsulinemia, insulin resistance, diabetes, syndrome X, dyslipidemia, menopausal vasomotor conditions, urinary incontinence, arteriosclerosis, libido enhancement, sexual dysfunction, depression, nervousness, irritability, stress, reduced mental energy and low self-esteem, improvement of cognitive function, endometriosis, polycystic ovary syndrome, counteracting preeclampsia, premenstrual syndrome, contraception, uterine fibroid disease, aortic smooth muscle cell proliferation, male hormone replacement, or ADAM.

The state of the prior art is that cancer therapy, for example, remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment

Art Unit: 1626

protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based on primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531). Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them.

The only direction or guidance present in the instant specification is the statement that "compounds of the current invention are modulators of the androgen receptor, glucocorticoid receptor, the mineralocorticoid receptor, and/or the progesterone receptor. Activity mediated through these oxosteroid nuclear receptors was determined using the following in vitro and in vivo assays." (page 34, lines 10 to 13). A description of progesterone receptor, androgen receptor, and glucocorticoid receptor fluorescence polarization assays, transient transfection assay and castrated male rat model follows (pages 35 to 39). There are no working examples present

Art Unit: 1626

for the treatment or prevention of any of the conditions or disorders recited in the claims.

The breadth of the claims is the treatment or prevention of any condition or disorder that responds to selective androgen receptor modulation and treatment or prevention of osteoporosis, muscle wasting, frailty, all cardiovascular diseases, breast cancer, uterine cancer, prostatic hyperplasia, prostate cancer, dyslipidemia, menopausal vasomotor conditions, urinary incontinence, arteriosclerosis, libido enhancement, depression, uterine fibroid disease, aortic smooth muscle cell proliferation, endometriosis, or ADAM comprising the administration of a compound according to claim 8.

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases would be benefited (treated) by and would then have to determine which of the claimed compounds would provide treatment of which disease, if any.

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired

Art Unit: 1626

pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for the treatment or prevention of any condition or disorder that responds to selective androgen receptor modulation and treatment or prevention of osteoporosis, muscle wasting, frailty, all cardiovascular diseases, breast cancer, uterine cancer, prostatic hyperplasia, prostate cancer, dyslipidemia, menopausal vasomotor conditions, urinary incontinence, arteriosclerosis, libido enhancement, depression, uterine fibroid disease, aortic smooth muscle cell proliferation, endometriosis, or ADAM comprising the administration of a compound according to claim 8. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

Genetech Inc. v. Novo Nordisk A/S 42 USPQ2d 1001 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Art Unit: 1626

Therefore, in view of the Wands factors and In re Fisher discussed above, to practice the claimed invention herein, one of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

No claim is allowed.

The references made of record and not relied upon show the state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fiona T. Powers whose telephone number is 571-272-0702. The examiner can normally be reached on Monday - Friday 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1626

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fiona T. Powers/
Primary Examiner, Art Unit 1626

Fiona T. Powers
Primary Examiner
Art Unit 1626

ftp
October 8, 2008